

JAPANESE MEDICAL MATERIAL

OSVAN

(Dimethyl-lauryl-benzyl-oxyethyl-ammonium-chloride)

297200

Report No. 240

3 July 1946

MEDICAL ANALYSIS SECTION
5250th Technical Intelligence Company
APO 500

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OSVAN

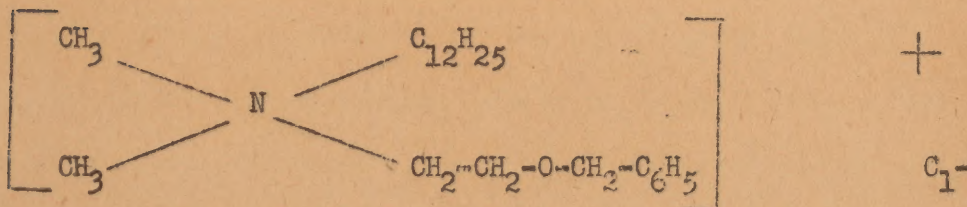
(Dimethyl-lauryl-benzyl-oxyethyl-ammonium chloride)

SOURCE: Tokyo, Japan.

IMPORTANCE: Not previously reported. An organic quaternary ammonium chloride employed as a detergent bactericide. No identical chemical product is listed in available standard American references.

DESCRIPTION: Seven hundred and fifty bright red tablets, each containing 0.2 grams of Osvan, are contained in a green glass bottle.

SUMMARY OF GENERAL INFORMATION: Osvan is claimed to be dimethyl-lauryl-benzyl-oxyethyl-ammonium chloride. The following chemical constitution is recorded:



Osvan is completely water-soluble detergent bactericide. Tests record that at the end of a 5 minute period it is active in the following dilutions against the organisms listed below:

| <u>Organism</u> | <u>Dilution</u> |
|-----------------|-----------------|
| B. coli | 1 - 20,000 |
| B. typhi | 1 - 40,000 |
| B. dysenteriae | 1 - 45,000 |
| Staphylococci | 1 - 10,000 |

An outline of the method of manufacture has been translated from the literature furnished by the manufacturer and is part of this report.

Other information furnished by the manufacturer has also been translated and embodied in the report. This includes the results of phenol coefficient tests against various bacteria, tissue irritation tests, etc. This translation also records some information on Osvan O, a similar detergent bactericide which consists chemically of dimethyl-octyl-lauryl-ammonium chloride and is active in even greater dilutions than Osvan.

In recent years, great impetus has been given to research on antiseptics of the quaternary ammonium halide group, many of which are surface active agents. Their solutions exhibit a low surface tension, good penetrating power and fine detergent action. Evaluation of Osvan and Osvan O can only be made after a thorough literature check.

PHOTOGRAPHS:

Figure 1 - Osvan, bottle containing tablets

Figure 2 - Osvan literature

Figure 3 - Osvan literature

Figure 4 - Osvan literature

Figure 5 - Osvan literature

Figure 6 - Osvan literature

Figure 7 - Osvan literature

Figure 8 - Osvan literature

Figure 9 - Osvan literature

Figure 10 - Osvan literature

Figure 11 - Osvan literature



報告用箋

Osvan

武田薬品工業株式会社

消毒用陽性石、換イオスバン（4メチルアミン）
 ベネルキエチルアミン（名リッド）ノ製法

1. 「ラウリルアルコール」ヲ塩化亜鉛及塩酸ニ「ヨリ」
 「クロロド」ヲ製ス

2. 「4メチルアミン」ニ亜硝酸「ソーダ」塩酸及苛性「ソーダ」ヨリ
 「4メチルアミン」ヲ製ス之ヲ純アルル「溶液」トシテ使用ス
 「4メチルアミン」ニ無キ場合ニハ「ホルマリン」塩化「アミン」

3. 「クロホルム」及苛性「ソーダ」ヨリ「4メチルアミン」ヲ製ス
 「ラウリルクロロド」ヲ「4メチルアミン」ニ作用セシメテ「4メチル
 「ラウリルアミン」ヲ製ス

4. 「エチレンジクロロ」ト「クロルベンザル」トヲ結合セシメテ

此場合過剰ノエチレンジクロライドヲ使用ス。ベンジルオキシ
エチルアルコールトナシ、之ヲ均化チオニールト反応セシメテ
ベンジルオキシエチルクロリッドヲ製ス
5 次イデ溶媒及觸媒トシテ無水アルコールヲ用ヒ
ベンジルオキシエチルクロリッドヲメチルアミントテ
尿素ノ存在ニ加熱反応セシメテ、メチルアミン、
ベンジルオキシエチル、アセチルクロリッドヲ析出シ之ヲ
醋酸エチルシヨリ再結晶シ精製ス

逆性石鹼「オスバン・オー」の殺菌力検定書

醫學博士 森

英 雄

一、供試藥劑

武田研究所に於て製造したる「オスバン・オー」(デメチル、オク
チル、ラウリル、アンモニウムクロリド)にして水、アルコールに
證明に溶解す

醫服用として標準石炭酸及び獨逸バイエル製「ツエフイロール」を
使用せり但し「ツエフイロール」は液体なるを以て重湯煎上にて加
熱し蒸發乾固し用に臨みその一定量を溶解して用ひたり

二、檢定術式

日本公衆保健協會雜誌法に據る

供試菌は

普通大腸桿菌

チフス桿菌(傳V株)

赤痢本型菌

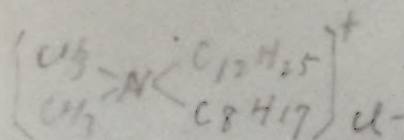


Figure 5- Osvan Literature

黄色葡萄狀球菌（辻井株）
 右の中葡萄狀菌は北膿部より分離せるものにして藥劑に對する抵抗
 力は對照試驗表に記する如く甚だ強き株なり
 一、實驗成績

對 照 試 驗

甲、標準石炭酸

| 藥劑濃度 | 作用時間 | 菌種 | | | | |
|------|------|----|-----|------|-----|------|
| | | | 大腸菌 | チフス菌 | 赤痢菌 | 葡萄狀菌 |
| 一對 | 六〇 | - | - | - | - | - |
| 七〇 | 七〇 | - | - | - | - | + |
| 八〇 | 八〇 | + | - | - | - | + |
| 九〇 | 九〇 | + | - | - | - | + |
| 一〇〇 | 一〇〇 | + | - | - | - | + |
| 一一〇 | 一一〇 | + | + | + | + | + |
| 一二〇 | 一二〇 | + | + | + | + | + |

Figure 6- Osvan Literature

乙、「ツエフィロール」

| 菌性 | 作用時間 | 藥劑濃度 | 一對 | 五〇〇〇 | 七五〇〇 | 一〇〇〇〇 | 一五〇〇〇 | 二〇〇〇〇 | 二五〇〇〇 | 三〇〇〇〇 | 三五〇〇〇 | 四〇〇〇〇 |
|------|------|------|----|------|------|-------|-------|-------|-------|-------|-------|-------|
| | | | | | | | | | | | | |
| 大腸菌 | 二五 | 五 | 一〇 | 一五 | - | - | - | - | - | - | - | - |
| チフス菌 | 二五 | 五 | 一〇 | 一五 | - | - | - | - | - | - | - | - |
| 赤痢菌 | 二五 | 五 | 一〇 | 一五 | - | - | - | - | - | - | - | - |
| 葡萄狀菌 | 二五 | 五 | 一〇 | 一五 | - | - | - | - | - | - | - | - |

Figure 7- Osvan Literature

「オスバン・オー」

本 試 験

| 一 五〇〇〇〇 | 一 四〇〇〇〇 | 一 三〇〇〇〇 | 一 二〇〇〇〇 | 一 一〇〇〇〇 | 一 〇〇〇〇〇 | 九 〇〇〇〇 | 八 〇〇〇〇 | 七 〇〇〇〇 | 六 〇〇〇〇 | 五 〇〇〇〇 | 一 對四〇〇〇〇 | 藥劑濃度 作用時間 | 菌種 |
|------------|------------|------------|------------|------------|------------|-----------|-----------|-----------|-----------|-----------|-------------|--------------|------|
| | | | | | | | | | | | | | |
| + | + | + | + | + | + | + | + | + | + | + | - | 二五五 | 大腸菌 |
| + | + | + | + | + | + | + | + | + | + | - | - | 五 | |
| + | + | + | + | + | + | + | + | + | - | - | - | 10 | |
| + | + | + | + | + | + | + | + | - | - | - | - | 15 | |
| + | + | + | + | + | + | + | + | + | - | - | - | 二五五 | チフス菌 |
| + | + | + | + | + | + | + | - | - | - | - | - | 五 | |
| + | + | + | + | - | - | - | - | - | - | - | - | 10 | |
| + | + | - | - | - | - | - | - | - | - | - | - | 15 | |
| + | + | + | + | + | + | + | - | - | - | - | - | 二五五 | 赤痢菌 |
| + | + | + | + | + | - | - | - | - | - | - | - | 五 | |
| + | + | + | - | - | - | - | - | - | - | - | - | 10 | |
| + | - | - | - | - | - | - | - | - | - | - | - | 15 | |
| + | + | + | + | + | + | + | + | + | + | + | - | 二五五 | 葡萄狀菌 |
| + | + | + | + | + | + | + | - | - | - | - | - | 五 | |
| + | + | + | + | + | + | - | - | - | - | - | - | 10 | |
| + | + | + | + | - | - | - | - | - | - | - | - | 15 | |

Figure 8- Osvan Literature

一、總括

右の成績表より當該細菌を五分間以内に殺滅し得る各藥劑の最高稀釋度を表示すれば次の如し

| 藥劑 | 菌種 | 對大腸菌 | 對チフス菌 | 對赤痢菌 | 對葡萄狀菌 |
|-----------|----|--------|--------|--------|--------|
| 石炭酸 | | 八〇 | 九〇 | 九〇 | 七〇 |
| 「ツエヒイロール」 | | 七五〇〇 | 二〇,〇〇〇 | 一〇,〇〇〇 | 五,〇〇〇 |
| 「オスバン・オー」 | | 五〇,〇〇〇 | 七〇,〇〇〇 | 九〇,〇〇〇 | 五〇,〇〇〇 |

尙右表の石炭酸稀釋度を壹とし之に對する各藥劑の比を求むれば

| 藥劑 | 菌種 | 對大腸菌 | 對チフス菌 | 對赤痢菌 | 對葡萄狀菌 |
|-----------|----|------|-------|-------|-------|
| 「ツエヒイロール」 | | 九四 | 二二二 | 一一一 | 七一 |
| 「オスバン・オー」 | | 六二五 | 七七八 | 一,〇〇〇 | 七一四 |

Figure 9- Osvan Literature

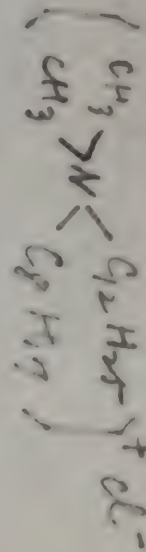
◎ 附

記

一、供試檢体ノ組成

「オスバン・オー」

化學構造式



一、供試檢体の粘膜刺激作用

各檢体の所定稀釋水溶液三滴宛を家兎に點眼し、血膜の發赤狀態及び分泌物の有無を検したるに次の如し

| 分泌物 | 發赤 | | 經過時間 | 稀釋倍數 | 藥劑 |
|-----------|-----|-----|------|------|-------|
| | 三時間 | 一時間 | 三時間 | 一時間 | |
| 「ツエフィロール」 | ++ | - | ++ | + | 1000 |
| | ++ | - | ++ | + | 2500 |
| | - | - | + | - | 5000 |
| | - | - | - | - | 10000 |
| 「オスバン・オー」 | ++ | - | ++ | + | 1000 |
| | - | - | + | - | 2500 |
| | - | - | - | - | 5000 |
| | - | - | - | - | 10000 |

Figure 11- Osvan Literature

附力赤ノ石炭炭層調査表タートクニニオスルオスルノ比ヲ示スルハ

| 種別 | 附力赤 | タートク | ニニ | オスル |
|------------|-----|------|------|-----|
| 「ツニファイワール」 | 九編 | 二二二 | 一一一 | 一一一 |
| 「オスバン・オ」 | 六二五 | 七七八 | 一〇〇〇 | 七一一 |
| 「オスバン」 | 五七五 | 四四四 | 三〇〇 | 一四六 |

Translation of Literature Furnished by Manufacturer

Certificate on the bacteriacidal action of inversive soap
"Osvan O" - By Hideo Mori, M.D.

Preparations used in test:

"Osvan O" prepared by the Takeda Research Laboratory is dimethyl octyl lauryl ammonium chloride, clearly soluble in water and alcohol. Standard phenol and zephirol "Bayer" are used for contrasting. However, since zephirol is a liquid it is evaporated on a water bath to obtain the solid constituents and when required a fixed quantity of the dried powder is dissolved and used.

Method of Certification:

This is in accordance with the method described in the magazine of Japanese Public Health Associations.

Bacteria used in test:

Common bacilli coli

Bacilli typhoid (V Mold-Infectious Disease Research Institution)

Bacilli dysentery - general type

Staphylococci, yellow (Tsuji mold)

Of the above bacteria, the staphylococci were separated from suppurations and the powerful resistant action of this mold against chemicals is shown in the following contrastive test table.

Results of Experiments:

Contrastive Tests

A - Standard Phenol

| Type of Bacteria Acting Time (Min.) | Bacilli Coli | Bacilli Typhoid | Bacilli Dysentery | Staphylococci |
|--|--------------|-----------------|----------------------|---------------|
| Strength of Preparations | 2.5 5 10 15 | 2.5 5 10 15 | 2.5 5 10 15 | 2.5 5 10 15 |
| 1 : 60 | - - - - | - - - - | - - - - | - - - - |
| 1 : 70 | - - - - | - - - - | - - - - | + - - - |
| 1 : 80 | + + - - | - - - - | - - - - | + + - - |
| 1 : 90 | + + - - | + - - - | + - - - | + + + - |
| 1 : 100 | + + + - | + + - - | + + + - | + + + + |
| 1 : 110 | + + + + | + + + - | + + + + | + + + + |
| 1 : 120 | + + + + | + + + + | + + + + | + + + + |

B-Zephnirol

| Type of Bacteria (Min.) Acting Time | Bacilli Coli | Bacilli Typhoid | Bacilli Dysentery | Staphylococci |
|--|--------------|-----------------|-------------------|---------------|
| Strength | 2.5 5 10 15 | 2.5 5 10 15 | 2.5 5 10 15 | 2.5 5 10 15 |
| 1 : 2500 | - - - - | - - - - | - - - - | - - - - |
| 1 : 5000 | - - - - | - - - - | - - - - | + - - - |
| 1 : 7500 | + - - - | - - - - | - - - - | + - - - |
| 1 : 10,000 | + - - - | - - - - | + - - - | + + - - |
| 1 : 15,000 | + + - - | - - - - | + - - - | + + + - |
| 1 : 20,000 | + + - - | + - - - | + + - - | + + + + |
| 1 : 25,000 | + + + - | + - - - | + + + - | + + + + |
| 1 : 30,000 | + + + + | + + - - | + + + + | + + + + |
| 1 : 35,000 | + + + + | + + + - | + + + + | + + + + |
| 1 : 40,000 | + + + + | + + + + | + + + + | + + + + |

C - Osvan O

| Type of Bacteria (Min.) Acting Time | Bacilli Coli | Bacilli Typhoid | Bacilli Dysentery | Staphylococci |
|---|--------------|-----------------|----------------------|---------------|
| | 2.5 5 10 15 | 2.5 5 10 15 | 2.5 5 10 15 | 2.5 5 10 15 |
| Strength | | | | |
| 1 : 40,000 | - - - - | - - - - | - - - - | - - - - |
| 1 : 50,000 | + - - - | - - - - | - - - - | + - - - |
| 1 : 60,000 | + + - - | - - - - | - - - - | + - - - |
| 1 : 70,000 | + + + - | + - - - | - - - - | + - - - |
| 1 : 80,000 | + + + + | + - - - | - - - - | + - - - |
| 1 : 90,000 | + + + + | + + - - | + - - - | + + - - |
| 1 : 100,000 | + + + + | + + - - | + - - - | + + + - |
| 1 : 110,000 | + + + + | + + - - | + + - - | + + + - |
| 1 : 120,000 | + + + + | + + + - | + + - - | + + + + |
| 1 : 130,000 | + + + + | + + + - | + + + - | + + + + |
| 1 : 140,000 | + + + + | + + + + | + + + - | + + + + |
| 1 : 150,000 | + + + + | + + + + | + + + + | + + + + |

Conclusions:

From the results of the above tables the maximum dilutions of each preparation which kill the bacteria within five minutes are as follows:

| Type of Bacteria Preparation | Bacilli Coli | Bacilli Typhoid | Bacilli Dysentery | Staphylococci |
|------------------------------|--------------|-----------------|-------------------|---------------|
| Phenol | 80 | 90 | 90 | 70 |
| Zephirol | 7500 | 20,000 | 10,000 | 5000 |
| Osvan O | 50,000 | 70,000 | 90,000 | 50,000 |

Comparison of each preparation against phenol whose dilution is assumed to be - 1.

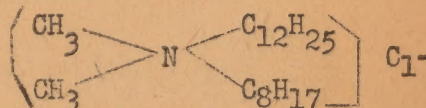
| Type of Bacteria Preparation | Bacilli Coli | Bacilli Typhoid | Bacilli Dysentery | Staphylococci |
|------------------------------|--------------|-----------------|-------------------|---------------|
| Zephirol | 94 | 222 | 111 | 71 |
| Osvan O | 625 | 778 | 1000 | 714 |

Additional Information

Composition of preparations used in test:

1. "Osvan O"

a. Chemical structure

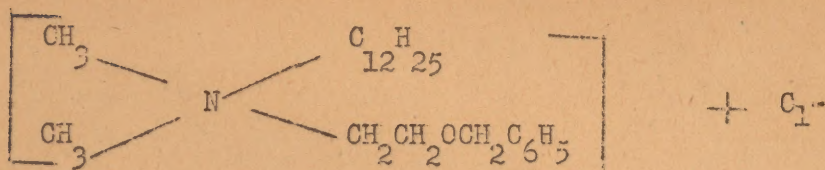


b. Irritating action upon mucous membrane.

Three drops of each preparation of fixed aqueous dilution were dropped into the eyes of rabbits and the state of reddishness of the conjunctive and the presence of secretions were examined.

| Elapsed Time | Preparation | | Zephirol | | | | Osvan O | | | |
|--------------|-------------|--|----------|------|------|--------|---------|------|------|--------|
| | Dilution | | 1000 | 2500 | 5000 | 10,000 | 1000 | 2500 | 5000 | 10,000 |
| Reddishness | 1 hour | | + | + | - | - | + | - | - | - |
| | 3 hours | | + | + | + | - | + | + | - | - |
| Secretion | 1 hour | | - | - | - | - | - | - | - | - |
| | 3 hours | | + | + | - | - | + | - | - | - |

2. "Osvan", (dimethyl lauryl benzyl oxyethyl ammonium chloride) is clearly soluble in water or alcohol.



The maximum dilution in which each preparation kills each type of bacteria within five minutes is shown as follows:

| Type of Bacteria Preparation | Bacilli Coli | Bacilli Typhoid | Bacilli Dysentery | Staphylococci |
|------------------------------|--------------|-----------------|-------------------|---------------|
| Phenol | 80 | 90 | 90 | 90 |
| Zephirol | 7500 | 20,000 | 10,000 | 5000 |
| Osvan | 20,000 | 40,000 | 45,000 | 10,000 |

Comparison of each preparation against a phenol dilution of 1.

| Type of Bacteria Preparation | Bacilli Coli | Bacilli Typhoid | Bacilli Dysentery | Staphylococci |
|------------------------------|--------------|-----------------|-------------------|---------------|
| Zephirol 0 | 94 | 222 | 111 | 71 |
| Osvan 0 | 625 | 778 | 1000 | 714 |
| Osvan | 375 | 444 | 500 | 146 |

Translation of Literature Furnished by Manufacturer

OSVAN

Takeda Pharmaceutical Co., Ltd.

Soap for disinfection "Osvan"

Dimethyl lauryl benzyloxyethyl ammonium chloride

Method of Preparation:

1. Add zinc chloride and hydrochloric acid to lauryl alcohol to form lauryl chloride.
2. Prepare dimethylamine from dimethylaniline, sodium nitrite, hydrochloric acid and caustic soda and dissolve it in pure alcohol. In case dimethylaniline is not available prepare dimethylamine from formalin, ammonium chloride, chloroform and caustic soda.
3. Prepare dimethyl laurylamine by the reaction of lauryl chloride and dimethylamine.
4. Combine ethyleneglycol and benzyl chloride (use excess ethyleneglycol) to prepare benzyloxy ethyl alcohol and react this with thionyl chloride to obtain benzyloxyethylchloride.
5. Using anhydrous alcohol as a solvent and catalyzer, heat benzyloxyethylchloride and dimethyl laurylamine in the presence of urea which will result in dimethyl lauryl benzyloxy ethyl ammonium chloride. Recrystallize this with ethyl acetate and purify.